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FROM THE ALLERGY DIVISION OF THE JEWISH HOSPITAL OF BROOKLYN

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ASTHMA AND HAY FEVER

Death From Bronchial Asthma. Williams, D. A., and Leopold, J. G.: Acta allergol. **14**: 83, 1959.

A clinical and pathologic study was made of 101 patients who died in status asthmaticus. More than two thirds in the group were females, and approximately 90 per cent of the deaths occurred in those past the age of 30. While the majority of the patients had had asthma for more than 10 years, about 20 per cent developed it in middle age and died from it within a few years. Postmortem studies were done in 54 cases. A striking and apparently previously unobserved pathologic finding was the fact that the cellular reaction of the bronchus and bronchioles did not extend to the terminal bronchioles in uncomplicated cases. M. C.

DERMATOLOGY

Polymorphous Light Eruption. A Discussion of Its Pathogenesis and the Therapeutic Action of the Antimalarials in This Disease. Shaffer, B., Cahn, M. M., and Levy, E. J.: J. Invest. Dermat. **32**: 363, 1959.

Polymorphous light eruption is considered to be an acquired, nonfamilial, allergic reaction occurring in persons with a past history of normal reactivity to sunlight, with lesions unlike those of ordinary sunburn. It was found in 40 per cent of such patients that specific reactions could be elicited after exposure to light between 2,900 and 3,100 Å. The peak of erythema occurred 48 to 96 hours after exposure and persisted for 7 to 14 days, after which papules often appeared. Pigmentation did not occur in these areas. Other wave lengths of light failed to produce this reaction. Test sites which were subsequently not exposed flared on exposure of other areas of skin to light. This suggested that an antigen-antibody system was involved in this reaction, although attempts at passive transfer of the reaction were unsuccessful. Treatment with chloroquine (Aralen) affected the photosensitivity favorably without altering normal "sunburn" reactions, contact-dermatitis due to poison ivy, histamine whealing, or Trichophyton inflammatory responses. The amounts of antimalarial drug present in the skin were found to be from 5 to 15 times higher in epidermis than in corium, but they were insufficient either to act as a sun barrier or to alter the spectrophotometric characteristics of the epidermis or corium. E. K.

Atopic Allergy and Atopic Dermatitis—A Discussion of Their Relationship. Strauss, J. S.: New York J. Med. **59**: 53, 1959.

Contact dermatitis was induced in a group of atopic male patients who showed skin test reactions to various atopens but did not have atopic dermatitis. The dermatitis was produced in each patient by the application of measured amounts of 3-pentadecylcatechol (PDC) after the minimal concentration needed to induce a positive response had been established. Each patient was then exposed for a month or two to the specific atopen to which he reacted by scratch test. The atopen was applied directly to the area of experimental dermatitis, injected subcutaneously at a distant site, or instilled into the nose. Controlled titrations with serial dilutions of PDC were carried out after the period of exposure to the specific atopen. The results of the tests showed that much weaker dilutions of PDC were now capable of inducing a positive contact reaction than had been needed originally. Frequently there were severe

flare-ups of previous patch test reactions following exposure to the atopen. The pruritus associated with the flare-ups caused scratching which brought about lichenification in some of the areas of patch testing. The atopens at no time produced new lesions. They were therefore only secondary offenders. The authors suggest that the administration of specific atopens to susceptible subjects may aggravate previous contact dermatitis sites and possibly may account for the flare-ups of naturally occurring atopic dermatitis. Desensitization may be beneficial in atopic dermatitis in that it might help to counteract secondary factors which help to aggravate the dermatitic reaction. R. W.

Inclusion of Antibiotics in Cosmetic Preparations. Nelson, C. T., and Sulzberger, M. B.: J. A. M. A. **169**: 1626, 1959.

The authors believe that the inclusion of antibiotics in cosmetics would have little value except for their deodorant action in reducing axillary odors. Disadvantages are enumerated, including contact dermatitis; nephrotoxicity from skin application of bacitracin, polymyxin B, neomycin, and tyrothricin; development of microbial resistance to frequently applied antibiotics; and development of moniliasis. D. G.

Prolonged Administration of Triamcinolone in Dermatologic Disorders. Therapeutic Efficacy and Side Effects. Kanof, N. B., Blau, S., Fleischmajer, R., and Meister, B.: A. M. A. Arch. Dermat. & Syph. **79**: 631, 1959.

Large doses of triamcinolone were administered to 75 patients, the majority of whom were suffering from either atopic or contact dermatitis. Patients were kept on therapy from 3 to 16 months; about 50 per cent of the group received daily treatment for at least 6 months. The average initial dose required to control symptoms was 22 to 24 mg. daily, while the maintenance dose was usually about 8 mg. daily. The drug was extremely effective therapeutically, and in only 2 cases was it necessary to stop the medication because of undesirable side reactions. Side reactions, such as moon facies and acne eruptions, occurred in approximately 10 per cent of the patients. Nausea, hypertrichosis, stomach pain, severe perspiration, glycosuria, vomiting, headaches, vertigo, mental depression, cellulitis, and stomach ulcer were encountered on rare occasions. R. W.

Dermatitis From Thermoplastic Tape. Kipping, H. F.: A. M. A. Arch. Dermat. & Syph. **80**: 348, 1959.

A 55-year-old male janitor developed a dermatitis on his back 3 weeks after he had worn a torn shirt repaired with thermoplastic tape. The plastic tape consisted of cloth impregnated with a vinyl resin, a stabilizer, and a plasticizer. A patch test performed with laundered tape yielded a 2-plus reaction at 48 hours. Similar cases of dermatitis have been found to be caused by the plasticizers and stabilizers present in vinyl resin wrist watch straps. R. W.

Poison Ivy Prophylaxis: Folklore or Scientific Medicine? Mitchell, W. F.: Ohio M. J. **55**: 797, 1959.

The alcohol-soluble fraction (oleoresin) of *Rhus toxicodendron,* combined with an inert filler, was incorporated into gelatin capsules and administered to 93 sensitive adults and children for prophylaxis against poison ivy dermatitis. Eighty-five (91 per cent) of these patients developed satisfactory protection. Side reactions consisted of 6 instances of mild dermatitis which

disappeared when the oleoresin was stopped and which did not recur when treatment was reinstituted. The preparation was found to retain its potency for one year. H. F.

Allergy to Montanoa Bipinntifida (Mayflower). Brum Negreiros, E., and Rizzini, T.: Alergia **6**: 304, 1959.

A 35-year-old white woman residing in Rio de Janeiro had developed redness, itching, and swelling of her right eyelid and a weeping rash of the right side of her face each June for the past 4 years. Patch tests were performed with the white flowers, the yellow flowers, and the petals of the *Montanoa bipinntifida* (mayflower). After 48 hours a 4-plus reaction was noted at the site of the yellow flower test, and 1-plus reactions were present at the sites of testing with the white flowers and the petals. Patch tests performed with both aqueous and ether extracts of these materials were negative. Control tests performed with turpentine, pyrethrum, zinia flowers and leaves (compositae), were negative except for a 1-plus reaction to pyrethrum. The local application of cortisone and silicone to a normal area of skin prior to the application of a patch test with mayflower failed to inhibit a positive reaction. J. Cortes

Allergic Eczematous Sensitivity to Aminophylline. Report of a Case. Baer, R., Cohen, A. H., and Neidorff, H.: A. M. A. Arch. Dermat. & Syph. **79**: 647, 1959.

A 58-year-old pharmacist was hospitalized on several occasions for an eczematoid eruption on the palms of his hands, followed by a generalized response. The lesions cleared rapidly following each hospitalization. On his fourth hospitalization, patch tests were made with nickel sulfate, tobacco, feathers, house dust, store dust, lanolin, *p*-dichlorbenzone, and pyrethrum. Store dust produced the only positive reactions. He failed to respond to usual dermatologic measures after discharge from the hospital.

After 3 years, it was noted that flare-ups occurred when the patient filled capsules with a mixture of papaverine, amobarbital, and aminophylline. When patch-tested with these 3 drugs, aminophylline gave a strongly positive reaction while the others gave negative reactions. Patch tests made with 1 per cent aqueous aminophylline, plain aminophylline, 1 per cent aqueous ethylenediamine dihydrochloride, ethylenediamine dihydrochloride as used in aminophylline, all yielded strongly positive patch reactions. Theophylline alone and 1 per cent theophylline in 70 per cent alcohol yielded negative patch reactions. The patient's eruption improved rapidly and he remained well upon avoiding exposure to aminophylline. Since ethylenediamine is used in various organic syntheses for the preparation of "dyes, inhibitors, rubber accelerators, fungicides, synthetic waxes, resins, insecticides, asphalt wetting agents, and certain pharmaceuticals," it is possible that the patient may have also obtained trace exposures to the ethylenediamine from these sources. R. W.

Zirconium Granulomas of the Glabrous Skin Following Treatment of Rhus Dermatitis. Report of Two Cases. Williams, R. M., and Skipworth, G. B.: A. M. A. Arch. Dermat. & Syph. **80**: 273, 1959.

A 50-year-old white woman with a Rhus dermatitis on the face, neck, and arms, was treated with repeated topical applications of zirconium oxide lotion, antihistamine ointments, and oral steroids. Pruritic vesicular eruptions recurred

in the areas of the original rash and were treated by repeated applications of the zirconium preparations. There was no past history of contact with zirconium through the use of a stick-type deodorant. Eighteen months following the application of the zirconium lotion, numerous reddish-brown, firm waxy papules developed over the flexor surfaces of both forearms and the anterior neck area. Laboratory studies, including skin tests with histoplasmin, coccidioidin, and PPD, were all negative. Histological examination of a papule revealed aggregates of epithelioid cells and Langhans' giant cells in the upper dermis. Special stains for acid-fast organisms and fungi were negative and no foreign material could be detected with polarized light. Patch tests performed with 4 per cent zirconium oxide and zirconium lotion, full strength, were negative at 48 and 72 hours. Application of 4 per cent zirconium oxide to an abraded area by the standard vaccination multiple pressure technique produced a reddish-brown nodule at 7 weeks. When the same procedure was repeated with a 1 to 100 dilution of 4 per cent zirconium oxide lotion, a reddish-brown papule resulted within 2 weeks. Biopsy of these nodules showed the same type of granulomatous lesions previously described. The eruption gradually cleared during a 12-month period after the patient stopped using the zirconium preparations.

The second patient was a 31-year-old Caucasian woman who developed a pruritic inflammatory eruption of reddish-brown papules confined to the axillae 2 months after using a commercial zirconium deodorant stick. The lesions did not respond well to topical steroid ointments or to superficial x-ray therapy. Biopsy specimens revealed a sarcoid-like granuloma confined to the upper corium. Patch tests with zirconium oxide lotion were negative; however, positive reactions were obtained following the application of a 1 to 100 dilution of 4 per cent zirconium oxide lotion by the multiple pressure technique. In 10 normal male subjects, the application by multiple pressure technique of both full strength and a 1 to 100 dilution of the 4 per cent zirconium oxide lotion yielded negative reactions at the end of a 2-week period.

R. W.

Reactions to Orally Administered Poison Ivy Extract. Swarts, W. B., and Rourke, T. A.: J. A. M. A. **170**: 1409, 1959.

Four members of a family who were sensitive to poison ivy took prophylactic doses of Aqua-Ivy tablets for 3 days. Three developed severe generalized pruritus and headache which lasted for one week. One developed bullae on the fingers. Another patient, a 14-year-old girl, after taking one tablet every other day for 3 days developed a swelling of the right wrist and elbow joints associated with a purpuric rash on the arms and chest. It was concluded that mass desensitization procedures without medical supervision are dangerous.

M. C.

MISCELLANEOUS ALLERGIES

Sensitivity Reactions to Intramuscular Injection of Benzathine Penicillin. Bernstein, S. H., and Houser, H. B.: New England J. Med. **260**: 747, 1959.

Two pilot studies, designed to determine the rate of sensitivity reactions to intramuscular benzathine penicillin, were carried out on military personnel. In the first study, a single intramuscular injection of 1,200,000 units of benzathine penicillin was administered to 306 airmen who were instructed to report immediately any signs of urticaria, joint swelling, or edema. Although approximately two thirds of these men had previously received penicillin, none gave a

history of drug sensitivity. A second injection was administered 40 days later to 100 men from this group without the occurrence of complaints suggestive of the development of penicillin sensitivity. The second pilot study which was more carefully controlled was carried out on 611 men, about two thirds of whom had previously received some form of penicillin without reaction. Alternate men received either 1,200,000 units of benzathine penicillin or sterile saline intramuscularly. Examinations and interviews were conducted 48 hours after injection and at weekly intervals for 4 weeks. Twenty-eight days later, a second injection of penicillin was given to those subjects who had reacted asymptomatically to the first dose. All other participants, including those who had developed sensitivity to the first penicillin injection, were given a saline injection. Serum sickness-like reactions consisting of angioneurotic edema, urticaria, and joint swelling occurred at a fairly predictable rate (1.7 and 2.3 per cent) in both study groups following a single intramuscular injection of 1,200,000 units of benzathine penicillin. However, the less severe symptoms were detected with greater frequency in the more carefully followed group. Drug sickness, urticaria, and pain at the injection site appeared attributable to benzathine penicillin, but symptoms of pruritus, arthralgia, fever, and rash occurred with equal frequency in both study and control groups. Since the relatively high reaction rate to 1,200,000 units of benzathine penicillin decreased when the dose was reduced, it was suggested that a lesser amount be employed for mass streptococcal-prophylaxis programs. H. S.

Further Experiences With Severe Allergic Reactions to Insect Stings. Mueller, H. L.: New England J. Med. **261**: 374, 1959.

Eighty-four cases of systemic reactions to insect bites were analyzed. Seventy-five per cent of the patients gave positive family or personal histories of allergy, and appeared to suffer more serious reactions than the 21 per cent who did not have allergic backgrounds. Identification of the stinging insect by the patient was found to be very unreliable. Skin tests performed with whole body insect extracts yielded multiple reactions in 89 per cent of the patients. Yellow jacket and hornet were the most powerful sensitizers. Desensitization therapy is recommended for all cases. The author advises using mixed whole-insect extracts of bee, wasp, hornet, and yellow jacket, starting with the dilution giving the "initial positive" skin reaction and slowly increasing to a maintenance dose of 0.2 to 0.3 ml. of a 1:100 dilution. Seventy-six per cent of the patients in the group were treated and 40 per cent of these suffered subsequent stings. With one exception, those who had reached maintenance doses of 0.15 ml. or greater of a 1:100 dilution of mixed extract, or those who had completed 3 years of treatment, were successfully protected against systemic reaction. H. S.

Fulminating Purpura With Gangrene of Lower Extremity Necessitating Amputation. Turin, R. D., Mandel, S., and Hornstein, L.: J. Pediat. **54**: 206, 1959.

Fulminating purpura (Schönlein-Henoch disease) is an infrequent expression of an anaphylactoid reaction which is probably related etiologically to bacterial hypersensitivity. Upper respiratory tract infections, particularly with hemolytic streptococci, frequently precede the onset of the syndrome, many of the features of which are also found in glomerulonephritis and rheumatism.

A case of Schönlein-Henoch disease occurring in a 3-year-old child is described. The initial symptoms of fever and lassitude were followed by a

diffuse erythemato-macular rash. Large ecchymotic and edematous areas appeared and were succeeded by widespread necrosis of the skin. The administration of antibiotics and steroids resulted in healing all the areas involved except for the left lower extremity which became gangrenous and had to be amputated. H. F.

Untoward Reaction to a New Ceruminolytic Agent. Daschbach, R. J.: A. M. A. J. Dis. Child. **98**: 776, 1959.

A 2-year-old boy with a background of bronchial asthma had several bouts of otitis media. Since his ear canals were occluded with wax, Cerumenex was instilled into them at night and they were plugged with cotton. Two days later there were swelling and itching of the ears and the auricles were markedly swollen and erythematous. This reaction spread to the face and upper portion of the neck. A month later Cerumenex was used again. Within several hours a similar reaction developed and the material had to be removed from the ear canals by irrigation. M. C.

Generalized Reactions to Bee and Wasp Stings. Seijffers, M.: Harefuah **56**: 309, 1959.

Twelve patients were hospitalized for severe reactions to wasp or honeybee stings. Only one member of the group was atopic. Eight of the patients gave a history of having been previously stung. The following symptoms and signs were observed: unconsciousness (8), shock (7), nausea and vomiting (5), restlessness (3), congested or swollen face (3), rash (2), fever (2), dyspnea (2), hot flushes (2), very severe pain (1), diarrhea (1), bloody diarrhea (1), hemiplegia and motor aphasia (1). Nine patients experienced severe immediate anaphylactic type reactions. No fatalities occurred.

The intravenous injection of calcium seemed to be effective in one case. Two patients in severe shock who failed to respond to epinephrine reacted favorably to intravenous infusion of norepinephrine. In 2 other patients norepinephrine was apparently lifesaving; one of them required it for 20 hours. The value of steroids and/or ACTH in 4 cases was inconclusive. I. Glazer

Penicillin-Sensitivity Reactions in Taiwan. Idsöe, O., and Wang, P. N.: Bull. World Health Organ. **18**: 323, 1958.

One hundred and six reactions were observed following penicillin administration in Taiwan between 1951 and 1955. Seventy-four were of the immediate anaphylactic type and 32 were of the delayed type. Among the cases of immediate reaction there were 12 fatalities and 19 patients with critical reactions who recovered. The delayed type reactions consisted mainly of urticaria. Ninety-eight per cent of the group with immediate reactions and 68 per cent of the group with delayed reactions had previously received penicillin without untoward effects. In both groups the time interval between previous penicillin administration and the reaction varied from 5 days to 7 years. I. Tsu Chao

Stillbirth Caused by Intradermal Penicillin Hypersensitivity Test. Tao, J., and Sung, C.: Chinese M. J. **76**: 174, 1958.

An intracutaneous test for penicillin sensitivity was performed on a 23-year-old parturient prior to the prophylactic administration of penicillin because

of early rupture of the fetal membranes. The test dose consisted of 0.1 ml. of a solution containing 200 units of penicillin. A systemic reaction consisting of tightness of the chest, numbness of the extremities, dyspnea, restlessness, and a diffuse scarlatiniform rash occurred within 5 minutes. Approximately 10 minutes after the introduction of the test the patient began to have labor pains and was delivered of a stillborn infant 36 minutes later. The fetal heartbeat had been regular and normal prior to the skin test. Soon after delivery the dyspnea disappeared and the skin rash faded in a few hours. A review of the past history revealed that the patient had had several previous penicillin injections and had once experienced a similar reaction. No personal or family history of atopy was obtained. T. Chao

Urinary Tract Allergy. Unger, D. L., Kubik, F., and Unger, L.: J. A. M. A. **170**: 1308, 1959.

A 49-year-old woman, under treatment for ragweed hayfever and asthma, had urinary burning, dysuria, and urgency for 10 years. These episodes recurred at any time of the year and lasted 2 to 3 hours at a time. The attacks were often associated with a rash on the face and dorsal surfaces of both hands. Cystoscopy revealed "cystitis" with generalized hyperemia of the bladder. Positive skin test reactions were obtained to pollen, molds, other inhalants, and several foods including cabbage, peanuts, soy bean, and filbert. The positive-reacting foods and all legumes were eliminated from the diet. The patient showed immediate improvement. Food trials revealed that nuts produced the rash and other foods the urinary symptoms. By avoiding the suspect foods, the patient has had no symptoms for 8 months. M. C.

Electrocardiogram of Patient in Anaphylactic Shock. Bernreiter, M.: J. A. M. A. **170**: 1629, 1959.

A 74-year-old man with no evidence of heart disease was given 600,000 units of penicillin as a prophylactic measure prior to a cataract operation. Within a few minutes he went into anaphylactic shock. He was given Adrenalin, steroids, and Levophed. An electrocardiogram taken 15 minutes after the penicillin administration, and while he was in severe shock, showed auricular fibrillation, multifocal ventricular ectopic beats, intraventricular conduction disturbance, and evidence of severe coronary insufficiency. A second electrocardiogram taken approximately 50 minutes after the first showed a remarkable change toward normal. A left ventricular strain pattern, a prolonged P-R interval, and evidence of coronary insufficiency were present. Although the patient made an uneventful cardiovascular recovery he developed a disorientation to time and place which was attributed to cerebral injury from the anoxia of shock. It was suggested that the myocardium and coronary circulation participate directly in anaphylaxis and that sudden death during such reactions may be explained on this basis. M. C.

Hypersensitivity to Immune Serum Globulin. Baybutt, J. E.: J. A. M. A. **171**: 415, 1959.

A 15-week-old normal infant was given 0.6 c.c. immune serum globulin, human, intramuscularly. Within 60 seconds, the baby became limp, generally erythematous, turned cyanotic, and stopped breathing. The patient was given 1 c.c. of Adrenalin which had to be repeated in 5 minutes. Wheezing and

frothing at the mouth developed. Steroids and other emergency measures were administered and after several hours, some improvement was noted. Both parents were highly allergic individuals. This appears to be the first case report of spontaneous hypersensitivity to immune serum globulin, human. M. C.

Anaphylactoid Reaction to Vancomycin. Rothenberg, H. J.: J. A. M. A. **171**: 1101, 1959.

A 17-year-old girl with acute penicillin-resistant staphylococcal endocarditis received an intravenous infusion of 1 gram of vancomycin in 250 c.c. of 5 per cent dextrose within 25 minutes. About 10 minutes after the infusion was concluded, she suddenly developed chest pain, dyspnea, pruritus, generalized urticaria, and angioedema. She became cyanotic and the pulse was "barely palpable." Epinephrine was given intravenously and subcutaneously and oxygen was administered. The patient was symptom-free 15 minutes later, although an expiratory wheeze was heard.

This reaction occurred after the first dose of the drug, and is the first reaction of this type to be reported with vancomycin. The patient had previously had an allergic reaction to a sulfonamide and subsequently to Novobiocin. M. C.

Anaphylactic Reaction to Chymotrypsin. Liebowitz, D., and Ritter, H., Jr.: J. A. M. A. **172**: 159, 1960.

A nonallergic 44-year-old man who had received 2 previous courses of chymotrypsin (Chymar) of 10 and 13 consecutive daily intramuscular injections, respectively, received another intramuscular dose of the medication 5 days following the end of the second course of treatment. Five minutes after this injection he became dyspneic, wheezed, and developed a generalized erythematous rash. Shortly thereafter frank pulmonary edema was evident and a generalized convulsion occurred along with loss of consciousness and apnea of about 30 seconds. Treatment with intravenous hydrocortisone and epinephrine resulted in eventual recovery.

This is the first report of an anaphylactic reaction to aqueous chymotrypsin. H. F.

PHARMACOLOGY, PHYSIOLOGY, AND PATHOLOGY

The Effectiveness of Tuberculo-Glycolipid as an Adjuvant in Eliciting Allergic Encephalomyelitis and Aspermatogenesis. Freund, J., and Stone, S. H.: J. Immunol. **82**: 560, 1959.

The adjuvant activity of Wax D, a lipoprotein extracted from killed human tubercle bacilli, was compared to that of whole tubercle bacillus in the induction of allergic encephalomyelitis and aspermatogenesis. Adult male guinea pigs of the Hartley strain were sensitized with either chloroform-purified material from guinea pig testis or rabbit spinal cord emulsified with varying amounts of *Mycobacterium tuberculosis* var. *hominis* (strain "Jamaica" 22), or of Wax D derived from these organisms in paraffin-oil-adjuvant emulsion. It was found that at least 0.015 mg. of tubercle bacilli was required to induce aspermatogenesis, whereas 0.1 mg. of Wax D was needed to produce a similar result. Similarly, at least 0.04 mg. of tubercle bacilli as compared to 0.4 mg. of wax was required to produce encephalomyelitis with death. The minimal amounts of adjuvant which caused encephalomyelitis with recovery was 0.02 mg. of

tubercle bacilli as compared to 0.2 mg. of Wax D. That Wax D was contaminated with whole or fragmented *Myco. tuberculosis* was demonstrated by sensitizing guinea pigs with Wax D or with whole, killed tubercle bacillus suspension and subsequently skin testing them with PPD. The minimum amount of Wax D capable of inducing tuberculin sensitivity in the guinea pigs was 0.2 mg. whereas animals sensitized with as little as 0.0004 mg. of *Myco. tuberculosis* showed positive PPD reactions.

From the above experiments it was seen that from 7 to 10 times more Wax D than tubercle bacillus was needed to induce aspermatogenesis and encephalomyelitis. However, the tubercle bacillus contains only from 6 to 8 per cent Wax D and, if the adjuvant action of the bacillus is due to its Wax D content, the wax is far more effective as an adjuvant when it is an integral part of the bacillus than when it is in its isolated form. D. Stein

Triamcinolone Myopathy. Williams, R. S., and Lond, M. B.: Lancet **1**: 698, 1959.

The author presented case reports of 3 patients who developed muscle damage following triamcinolone therapy. One of the patients had polyarteritis nodosa, one had asthma, and one scleroderma. About 2 to 3 weeks after starting the steroid the patients complained of heaviness and weakness of the legs and 2 were so weak that they had difficulty in supporting their own weight. None of the 3 patients had any sensory changes but one patient did have a diminution of his reflexes. After being switched from triamcinolone to prednisolone, 2 of the patients noted a marked improvement in muscle power within 1 week. Metabolic studies showed a similar nitrogen balance on triamcinolone and prednisolone in 2 cases. In the third case, there was a small loss of 3.2 grams of nitrogen over a 6-day period on triamcinolone as compared to a gain of 0.5 gram daily over a similar period with prednisolone. Calcium excretion was similarly affected by the two steroids and all the serum electrolytes were normal throughout the studies. Electromyogram studies carried out on all 3 patients showed that primary muscle fiber damage had occurred. A neuromyopathic lesion characteristic of polymyositis was present. All patients had a negative neostigmine test. Biopsies taken on 2 patients revealed uneven atrophy of the muscle fibers but the distribution of the atrophy did not suggest a neurogenic origin. Although metabolic studies showed no significant difference in protein catabolic activity between triamcinolone and prednisolone given in comparable doses, electromyograms definitely established evidence of a primary muscle fiber lesion in patients receiving triamcinolone. R. W.

IMMUNOLOGY

In Vivo Fixation of Antibodies in the Adrenal. Hiramoto, R., Yagi, Y., and Pressman, D.: Proc. Soc. Exper. Biol. & Med. **98**: 870, 1958.

Fixation of anti-kidney antibodies in the adrenal gland has been previously demonstrated by radio-labeled antibody techniques. In this study, an immunohistochemical fluorescent stain method was used to determine more precisely the site of antibody localization in the gland. Rats were injected intravenously with rabbit anti-rat kidney serum, the globulin fraction of which had been labeled with I^{131} (G-anti-RK). The animals were sacrificed and perfused 18 hours after injection of antibody. Radioactivity measurements were made on the perfused organs when required, and the tissue was quickly frozen. Tissue

sections were stained with fluorescein- or rhodamine-labeled horse anti-rabbit globulin serum. Rats were injected with varying quantities of I^{131} labelled G-anti-RK in order to determine the concentration of G-anti-RK required in the adrenals for detection by the fluorescein antibody. Control animals received radioactive normal globulins (GNS). Radioactive assay by counting revealed that rats receiving doses of 6.9 mg. of radio-labeled G-anti-RK fixed antibody to the extent of 90 μg and 26 μg protein per gram of tissue for the adrenals and kidneys, respectively. Comparable, but greater, localization was noted after injection of 15 mg. G-anti-RK. Staining of the adrenals was readily obtained at both concentrations. Control animals given 15 mg. GNS localized 20 μg per gram of adrenals and 15 μg per gram of kidneys, but this was not detectable by fluorescein-labeled antibody. Some localization was noted in both organs after injection of only 2.2 mg. G-anti-RK, but positive staining by the fluorescein procedure appeared only in the kidneys. "Although the average concentration of localized antibody was greater in the adrenal than in the kidney, actual concentration of antibody globulin at site of fixation was less since antibody could be detected only in kidney at lowest amounts injected."

After the limit of detection had been demonstrated, unlabeled G-anti-RK was used in studies of the histologic site of the localized antibody. Tissues from rats which had been injected with globulin from pooled normal rabbit sera were used as controls. When small amounts, 4 to 7 mg. G-anti-RK, were administered, fixation of antibody took place along the vessels and sinusoids of the cortex, just inside the capsule. Only when doses of 15 mg. or greater were injected did localization occur farther inside, giving the appearance that antibody was being cleared. No fixation was observed in the capsule, or in the large polygonal parenchymal cells. Although the medulla does contain substances which react with anti-kidney antibody in vitro, no staining was discernible in the medulla. It is suggested that certain derangements of adrenal function may be due to the effect of anti-kidney antibodies. H. S.

Relationship of Circulating Antigen-Antibody Complexes, Antigen Elimination, and Complement Fixation in Serum Sickness. Weigle, W. O., and Dixon, F. J.: Proc. Soc. Exper. Biol. & Med. **99**: 226, 1958.

Rapid immune elimination of antigen usually accompanies the development of symptoms and lesions of experimental and clinical serum sickness. In this study, attempts were made to correlate the extent of the associated morphologic manifestations with the level and persistence of antigen-antibody complexes and the fall in complement activity.

Twenty-six albino rabbits were injected intravenously with 250 mg. per kilogram of bovine serum albumin (BSA), trace-labeled with I^{131} (I^{131} BSA). The sera were analyzed every 1 or 2 days for total I^{131} BSA, I^{131} BSA bound to globulin, and complement. Rabbits showing complete immune elimination of antigen by the sixteenth day were sacrificed 1 day later. One rabbit showing no immune elimination was sacrificed on the fourteenth day and another which did not show immune elimination until the eighteenth day was sacrificed the next day. All other animals were sacrificed on the sixteenth or seventeenth day. Sections of tissue obtained at autopsy were studied to determine the incidence and degree of glomerulonephritis, arteritis, and endocarditis. Glomerular alterations were used as a basis for correlation of morphologic and serologic developments.

"Almost all rabbits responded to large injections of BSA by making antibodies capable of forming complexes with circulating antigen yet only ⅔ of

them developed significant lesions.'' The most severe morphologic changes of serum sickness tended to occur in those animals in which complexes formed and were rapidly eliminated. However, in 3 animals with relatively early elimination of antigen, there were few, if any, lesions, and in 2 of 4 animals showing no immune antigen elimination there were significant lesions of glomerulonephritis. Although complement levels declined in all animals showing an immune elimination of antigen, complement did not appear to be utilized in some animals which developed lesions, and, in some animals showing a fall in complement, no lesions were found. Therefore no consistent correlation could be made between the levels of antigen-antibody complexes in the sera or the rate of utilization of complement and either the development or severity of lesions of serum sickness. The possibility that other factors might be involved or that complexes might vary in their nature and pathogenicity was suggested. H. S.

Antigenicity of Steroid-Protein Conjugates. Beiser, S. M., Erlanger, B. F., Agate, F. J., Jr., and Lieberman, S.: Science **129**: 564, 1959.

Conjugates were formed by coupling testosterone, cortisone, desoxycorticosterone, estrone, and progesterone to bovine serum albumin (BSA). Antisera were prepared by injecting rabbits with alum-precipitates of these conjugates. After absorption with BSA, the antisera were found not only to react with the steroid-protein conjugate used for immunization, but to cross-react with the other conjugates. The steroid specificity of the antisera was studied with the hapten-inhibition technique. Each steroid was prepared as a hapten with succinate or O-(carboxymethyl) oxime and then incubated with the antiserum prior to the addition of the homologous antigen. By comparing the precipitate formed in the presence of the hapten with the precipitate formed without the hapten, the effectiveness of each hapten in inhibiting precipitation was calculated. Since each antigen-antibody system was inhibited best by the homologous hapten, the steroid specificity of the antisera was demonstrated. The effect of chemical changes of the homologous hapten on its effectiveness as an inhibitor of an antigen-antibody system was also studied. The results of this study yielded information on the chemical basis of specificity of that antigen-antibody reaction. B. S.

Two Antigenically Different γ-Globulins in Domestic Rabbits Revealed by Isoprecipitins. Dray, S., and Young, G. O.: Science **129**: 1023, 1959.

Previous studies have indicated that components of serum from individual rabbits are antigenic in other rabbits. These isoantibodies were produced by the injection of serum plus adjuvants and were detected by the precipitin reaction and by passive cutaneous anaphylaxis in the guinea pig. In the present report, the authors investigated this phenomenon by double diffusion agar-gel techniques, micro-immunoelectrophoresis, and a modification of Björklund's inhibition technique. These studies revealed the presence of two different γ-globulin antigens in rabbit sera, designated RGG-I and RGG-II. Sera from individual rabbits contained either RGG-I or RGG-II, or a combination of both.

An analysis was made of the sera of 500 rabbits of several breeds and from different sources. Twenty-four rabbits showed only RGG-I in their sera, 379 rabbits showed only RGG-II, and 97 rabbits showed both RGG-I and RGG-II in their sera. None of the rabbits lacked both γ-globulin specificities. Preliminary cross immunization studies done among the three known groups of rabbits have thus far failed to reveal a third γ-globulin specificity. B. S.

Effect of 6-Mercaptopurine on Antibody Production. Schwartz, R., Stack, J., and Dameshek, W.: Proc. Soc. Exper. Biol. & Med. **99**: 164, 1958.

The association of a modified immune response with the successful transplantation of homografts has stimulated interest in the various methods of altering antibody formation. In this study, 6-mercaptopurine (6-MP), an antagonist of nucleic acid metabolism, when given simultaneously with antigen profoundly suppressed the antibody response to a purified protein antigen.

Rabbits were injected intramuscularly with 50 mg. of crystalline bovine albumin (BSA) 3 times weekly for 2 weeks. The first day of BSA administration was counted as day 0. A schedule was devised in which a dose of 3 mg. per kilogram of 6-MP was administered at recorded intervals to groups of these experimental animals, beginning either before, during, or after antigenic stimulation. Antibody determinations, made by the tannic acid hemagglutination technique of Stavitsky, were carried out on blood samples.

"Low titers of antibody could be detected in the control group by day +4, with a peak titer at about day +16; thereafter a plateau persisted through the last bleeding at day +38." Introduction of 6-MP prior to antigenic stimulation, from days −7 to +4, resulted in only a slight delay in antibody production. However, when the antimetabolite was given simultaneously with the antigen, from days 0 to +11, antibody levels were suppressed significantly. Treatment with 6-MP from days 0 to +21 abolished the antibody response completely. Although temporary cessation of response occurred when 6-MP was given from days +7 to +18, its administration at the height of antibody response, from days +18 to +29, produced no effect on the titer in the serum. Hence, it was tentatively concluded that the action of 6-MP is on the primary antibody response, rather than on the anamnestic response. H. S.

Delayed Hypersensitivity in Mice: Its Detection by Skin Tests and Its Passive Transfer. Crowle, A. J.: Science **130**: 159, 1959.

A group of white mice were injected intraperitoneally twice at weekly intervals with a water-in-oil emulsion containing living tubercle bacilli and twice-crystallized ovalbumin. Another group of mice was injected similarly with emulsion alone. Two weeks after the second injection, all control and most of the test mice were injected intracutaneously with 0.01 ml. of a 1 per cent ovalbumin solution. Between 3 and 6 hours later, the sensitized mice developed edema and occasionally petechiae at the site of the intracutaneous injection. Between 24 and 48 hours after intracutaneous injection, definite evidence of a delayed-type skin reaction developed in the sensitized mice, consisting of induration, skin thickening and, in many instances, central necrosis.

Four of the sensitized mice which had not received an intracutaneous injection and 5 normal mice were sacrificed and used as cell and serum donors. Cell suspensions were prepared from the thymus glands and their attached lymph nodes. The cells and sera from each group of mice were pooled. Normal recipient mice were injected intraperitoneally with 0.1 ml. of serum or 0.4 ml. of cell suspension. The serum recipients were challenged intracutaneously with 0.01 ml. of 1 per cent ovalbumin solution 24 hours after the serum injection while the cell recipients were challenged after an interval of 48 hours. The recipients of normal cells or serum failed to react to the ovalbumin challenge. The recipients of sensitized serum developed edematous reactions 3 hours after challenge, which disappeared after 6 hours. The cell recipients showed no reactions until the 6-hour reading, when induration began and continued to develop through the forty-eighth hour. All these mice showed central necrosis.

This is the first report of successful passive transfer of delayed hypersensitivity in mice. B. S.

Simultaneous Placental Transfer of Factors Responsible for L. E. Cell Formation and Thrombocytopenia. Nathan, D. J., and Snapper, I.: Am. J. Med. **25**: 647, 1958.

A 15-year-old white girl, with partially controlled systemic lupus erythematus (S.L.E.), experienced a flare-up in the last trimester of her pregnancy. She went into labor and spontaneously delivered a 3 pound male child. Two days later, it was noted that the mother's blood clot failed to retract and the platelet count was 45,000 per cubic millimeter. L.E. preparations remained strongly positive. Within 24 hours after the delivery, her temperature rose to 101° F. and she was started on a therapeutic regime of prednisone 30 mg. daily and penicillin. The temperature continued to spike despite maintenance doses of prednisone which were increased to 60 mg. daily. The lupus erythematosus did not subside until she was put on 200 mg. hydrocortisone daily. Aside from prematurity, the child appeared normal at birth. His platelet count at the end of 24 hours of life was 30,000 per cubic millimeter. There was no appreciable clot retraction at the end of 4 hours. Examination of his blood on the second day disclosed weak but definite L.E. cell formation. Within a week, the baby's blood showed clot retraction and a platelet count of 92,000 per cubic millimeter. His platelet count reached normal proportions in about a month. Examination of the blood of the mother and baby taken 2 days after delivery showed the presence of platelet agglutinins. Hence, this study demonstrated the placental transfer of humoral factors responsible for L.E. cell formation and congenital thrombocytopenia in a patient with S.L.E. E. W.

The Sites of Antibody Production. Sulitzeanu, D.: Harefuah **57**: 29, 1959.

Rabbits hyperimmune to the polysaccharide Pn III were injected with aminoacids labeled with C^{14} and their incorporation in the antibodies was followed. The animals were sacrificed at different intervals after the injection of the radioactive substance and following a rapid perfusion in Ringer's solution the organs were removed, their antibodies extracted, and radioactivity determined.

In order to distinguish between the intracellular, the antibodies and the extracellular antibodies left in the organs in spite of the diffusion the following technique was used. A few days before the experiment was begun the rabbits were injected with a definite amount of homologous antibodies (anti Pn III) labeled with I^{131}. These antibodies were mixed in the rabbit with those it produced and thus it was possible to distinguish the intracellular part from the extracellular part of the produced antibodies incorporating C^{14} amino acids. The author concluded that the antibodies were produced directly from the free amino acids of the organs which are in rapid equilibrium with the amino acids of the plasma. Antibody molecules formed in the organs are secreted into the blood stream within 15 minutes after being formed. The relative contribution of several organs to the total pool of circulating antibody and the turnover time of the intracellular antibody of these organs was determined. The lung contained the largest amount of antibodies (their turnover time was 2 hours) and contributed the largest share to the serum pool. Bone marrow contained the second largest amount and the spleen only a small amount. The spleen antibody appeared to be synthesized at a greater rate than that of the lung. I. G.

ANAPHYLAXIS

Passive Anaphylaxis in the Guinea Pig and Its Inhibition by an Extraneous Antigen-Antibody Reaction. Pruzansky, J., Feinberg, S. M., and Kenniebrew, A.: J. Immunol. **82**: 497, 1959.

The relationship of antigen and antibody concentration was studied in passive anaphylaxis of the guinea pig challenged by aerosolized antigen.

Guinea pigs were passively sensitized intravenously with guinea pig anti-egg albumin (EA) serum, or with guinea pig antibovine gamma globulin (BGG) serum and challenged with aerosolized homologous antigen (1 per cent). The time required to elicit end point symptoms of spasmodic breathing and/or cough ("anaphylaxis time") was progressively shortened to a lower limit of 60 seconds by increasing the concentration of antigen. Similarly, a progressive shortening of anaphylaxis time was found when the antibody concentration was increased. Guinea pigs passively sensitized with anti-BGG were injected intraperitoneally with EA and one hour later received an intravenous injection of anti-EA. The in vivo antigen-antibody reaction resulted in refractoriness to anaphylaxis, as evidenced by prolongation of anaphylaxis time upon subsequent challenge one hour later with BGG aerosol. The supernate from an in vitro nonrelated antigen-antibody system also had an inhibitory effect on anaphylaxis whereas injection of washed precipitate of unrelated systems afforded no protection. The protective effect of an extraneous antigen-antibody reaction could be overcome by challenge with higher concentrations of homologous antigen (up to 4 per cent) and also by injection of fresh pooled guinea pig serum one hour before challenge.

Two possible mechanisms for the inhibition of anaphylaxis are suggested: (1) tissue permeability to challenging doses of standard concentration of homologous antigen is reduced by the interaction of extraneous antigen with antibody; and (2) an inhibitor of a precursor to anaphylaxis may be formed by the interaction of extraneous antigen with antibody. D. Stein

MISCELLANEOUS

Effect of Polluted Los Angeles Air (Smog) on Lung Volume Measurements. Motley, H. L., Smart, R. H., and Leftwich, C. I.: J. A. M. A. **171**: 1469, 1959.

Smog in Los Angeles results mainly from the operation of three million automobiles in a city hemmed in by mountains on three sides. It is produced by chemical reactions among the pollutants of the automobile exhaust which include ozone, oxides of nitrogen, sulfur dioxide, and carbon monoxide. Other constituents, such as aldehydes and organic acids, may be even more harmful. Pulmonary function studies were done on 66 volunteers, 46 of whom had pulmonary emphysema and 4 of whom had bronchial asthma. Emphysema subjects, after breathing either smoggy air or clear Los Angeles air, were allowed to breathe air filtered through activated carbon. They showed significant objective quantitative improvement in ventilating characteristics, especially a decrease in the volume of residual air. The severity of the emphysema was aggravated by smog, and this effect could be reversed by breathing filtered air for 40 hours. The use of activated carbon filters is advised in the homes and in the offices of emphysematous patients. M. C.

Rapid Slide Technique for Double Diffusion Agar Precipitin Test. Yakulis, V. J., and Heller, P.: Am. J. Clin. Path. **31**: 323, 1959.

Readable precipitin lines were obtained within 16 to 18 hours by a micro-technique adaption of Ouchterlony diffusion. A 25 cm. square is outlined with paint pencil on a microscope slide. A thin layer of agar is applied within the square, and 3 mm. cores are cut out in an appropriate pattern. The base of each core is lightly coated with agar and 15 to 20 lambda of reactant placed in the resultant wells. Incubation is carried out in a Petri dish over moistened filter paper at 37° C. for 12 to 18 hours. For permanent reference, fixative may be applied to the preparation after the precipitin lines are formed. No difficulty was encountered in reading crossing and merging of lines or spur formation. E. K.

The Use of Purified Antigens in the Diagnosis of Clonorchiasis Sinensis by Means of Intradermal and Complement Fixation Tests. Sadun, E. H., Walton, B. C., Buck, A. A., and Lee, B. K.: J. Parasitol. **45**: 129, 1959.

Intact adult worms of *Clonorchiasis sinensis* were washed, frozen, and lyophilized. From these were obtained a crude fat-free antigen (CC), a lipid-free borate buffer extract (CTP), an acid-soluble protein (CM), and an acid-insoluble but alkali-soluble protein (CM-ins). The most reliable results were observed with the CM extract. All but 3 of 132 patients with known clonorchiasis responded with immediate wheal reactions following an intracutaneous test with CM extract, while tests on only 2 of 120 trematode-free persons were positive. Cross reaction with paragonimiasis and schistosomiasis was moderate. The CM-ins and CTP preparations produced complement fixation antigens in 23 of 25 patients with clonorchiasis, and only one positive reaction among 20 sera from trematode-free persons. Cross reactions were again noted with paragonimiasis, schistosomiasis, and unduly aged sera from tuberculosis and leptospirosis victims. E. K.